Antimicrobial Stewardship: *Introduction to the CMIB.*

For the Veterinary Professional
Outline

• What is the Compendium of Medicating Ingredients Brochures (CMIB)?
• What is the purpose of CMIB?
• Which changes have been made to the structure of the CMIB?
• An example of how to use the document to prescribe a medicated feed
What is the CMIB?

A regulatory document featuring a collection of **Medicated Ingredient Brochures (MIB)** which provide information for all Health Canada approved in-feed medications.

Each active ingredient has its own MIB based on approved product labels and includes:

- Approved claims for each medication
- Drug levels (dosages) for each claim
- Information required to appear on the medicated feed label
- Any restrictions for the use of the medication, such as the withdrawal time
Purpose of the CMIB

• Feeds manufactured with medicated ingredients that are Over-the-Counter (OTC) and pursuant to the CMIB will not require a veterinary prescription prior to manufacture or sale (except in Quebec)

• Feeds manufactured with a Prescription medicated ingredient according to the CMIB can be mixed prior to the receipt of a veterinary prescription i.e., “floor stocked” and made available for sale with a valid veterinary prescription

• Feeds manufactured with a medicated ingredient that does not follow the CMIB (i.e., off-label) will require a veterinary prescription prior to manufacture.
Purpose of the CMIB

The CMIB is a reference document for use by all stakeholders which describes which medications have been approved to be mixed into feeds, under what circumstances and how they are to be mixed to facilitate the manufacture of feeds prior to receiving a veterinary prescription (i.e., floor-stocked).

– Section 14 part (b) of the Feeds Regulations states:

*A feed shall not contain medicating ingredients of a brand, at a level or for a purpose or species other than as set out in the Compendium of Medicating Ingredients Brochures unless the feed is a veterinary prescription feed.*
Changes to the CMIB-2018

The introduction of new regulations to combat antimicrobial resistance have triggered a number of changes to the CMIB

<table>
<thead>
<tr>
<th>Prior to 2018</th>
<th>2018 and Beyond</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth promotion claims present</td>
<td>Growth promotion claims removed, including removal of products with solely GP claims</td>
</tr>
<tr>
<td>Only OTC medications</td>
<td>Both OTC and Prescription products</td>
</tr>
<tr>
<td>No DIN numbers listed</td>
<td>DIN numbers listed for all products</td>
</tr>
<tr>
<td>MIBs listed by number code, ex. tylosin was #80</td>
<td>MIBs listed by letter code, ex. tylosin is now TYL (based on active)</td>
</tr>
</tbody>
</table>
How the CMIB is structured?

The CMIB contains an introductory chapter and MIBs that are searchable in the following ways:

• By active ingredient
• By brand name
• By livestock species
• By sponsor/manufacturer

Note: The CMIB is a living document that is updated regularly. It is your responsibility to ensure you are referencing the most up-to-date MIB.
How each MIB is structured

Each MIB within the compendium is organized into three sections:

1. Introductory profile
2. Claim (indication) – with directions for use and restrictions
3. Accepted compatibilities
1. The introductory profile

- Prescription status (i.e., Prescription or OTC)
- Active ingredient
- Species of livestock for which the MIB is approved
- Table of approved claims for which the medication may be used
- Approved brands (of DIN premixes that contain the medicating ingredient)
- Approved form of feed (granular, meal or pellet) – where applicable
2. Claim (Indication)

- Level of medication in the finished feed
  - Expressed as a mg of active per kg of complete feed (%)
  - May also be specified as kg/head/day, per kg of body weight
- Directions for feeding – length of time to feed the medicated feed
- Any additional directions to the feed manufacturer and/or the end-user
- Warnings (human safety) and Cautions (animal safety)
  - Warnings and cautions must appear on the label for the finished feed, except where noted in the individual MIB.
3. Accepted compatibilities

- Compatibilities are medications that have been approved for use concurrently in feed, based on safety and a lack of drug interference.
- Accepted compatibilities are species and claim-specific.
- Approved compatibilities are listed in a table at the end of the MIB section for that species.
- Directions for use and restrictions for each compatible medication must be followed.
- When combining multiple medications the longest withdrawal time must be followed and must appear on the label for the finished feed (only one withdrawal time should be listed on the feed label).
How to use the CMIB

• The following is a demonstration using the CMIB for:
  – Prescribing a CMIB-compliant medicated feed
  – Prescribing an extra-label medicated feed
Our scenario

A veterinarian wishes to issue a prescription for a “Beef Supplement” medicated with chlortetracycline hydrochloride (listed as CTC in the CMIB) as an aid in the prevention of foot rot as indicated in the CMIB.

Note that CTC is a medically important antimicrobial.

The veterinarian’s client - a local beef producer - currently purchases a non-medicated beef premix at a local feed manufacturing facility and mixes it at 25 kg per tonne of complete feed in his on-farm mixer.

The prescription will allow his client to purchase this same supplement but with the addition of the medically important antimicrobial CTC, which as of December 1, 2018 requires a veterinary prescription to be issued before the medicated feed can be purchased.
CFIA website (www.inspection.gc.ca)
Under “Animals” click on “Feeds”
Click on “CMIB Table of Contents”
Which index to use?
We can find “Chlortetracycline hydrochloride” (CTC) using any of the four indexes.
To find CTC using:
Index of medicating ingredients brochures by name

**Index contains:**
- link by MIB code – “CTC”
- Name of medicating ingredient - Chlortetracycline hydrochloride
- Status - Veterinary prescription
- Approved brand(s) – 4 available
- Date of revision of MIB – 2018-04

<table>
<thead>
<tr>
<th>MIB code</th>
<th>Name of medicating Ingredient</th>
<th>Status</th>
<th>Name of approved brand(s)</th>
<th>Data of revision</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMP</td>
<td>Amprolium</td>
<td>Over the-counter</td>
<td>Amprol Feed Premix</td>
<td>2017-10</td>
</tr>
</tbody>
</table>
| AVI      | Avilamycin                      | Veterinary prescription | 1. Surmax 100 Premix
2. Surmax 200 Premix | 2015-04         |
| BACN-M   | Bacitracin (as bacitracin methylene Disalicylate) | Veterinary prescription | 1. BMD 110 G
2. Bacitracin MD | 2016-06 |
| BACN-Z   | Bacitracin (as zinc bacitracin)  | Veterinary prescription | 1. Albac 110 Zinc Bacitracin Premix
2. Zinc Bacitracin 110 | 2016-04 |
| RPM      | Rambergmycine                   | Over the-counter | Flavomycin 4 Antibiotic Premix | 2006-09         |
| OLO      | Clopidol                        | Over the-counter | Coyden 25 Anticoagulant Premix | 2017-07         |
| CSP      | Chlortetracycline hydrochloride, Sulfamethazine and Pantomycin | Veterinary prescription | 1. Aureo S-P 250 G Granular Medicated Premix
2. Aureomax 525 G Granular Medicated Premix
3. Chlor 260 Medicated Premix
4. Super Chlor 250 Medicated Premix
5. Super Chlorosol-260 Drug Premix | 2018-04 |
| CTC      | Chlortetracycline hydrochloride | Veterinary prescription | 1. Aureomycin 220 G Granular Medicated Premix
2. Chlor 50 Medicated Feed Premix
3. Chlor 100 Granular Medicated Premix
4. Daracin 22% Granular Premix | 2015-04 |
### Index of medicating ingredient brochures by name

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Looking for related documents? [Search for related documents in the Guidance Document Repository](#)

**Date of revision: November 2018**

#### Medicating ingredient brochures by name

<table>
<thead>
<tr>
<th>MIB code</th>
<th>Name of medicating ingredient</th>
<th>Status</th>
<th>Name of approved brand(s)</th>
<th>Date of revision</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMP</td>
<td>Amprolium</td>
<td>Over the Counter</td>
<td>Amprolium Feed Premix</td>
<td>2017-10</td>
</tr>
</tbody>
</table>
| CTC      | Chlortetracycline hydrochloride                | Veterinary prescription | 1. Aureomycin 220 G Granular Medicated Premix  
2. Chlor 50 Medicated Feed Premix  
3. Chlor 100 Granular Medicated Premix  
4. Deracin 22% Granular Premix | 2018-04         |
To find CTC using: Index of medicating ingredients by brand name

Click on “Index of medicating ingredients by brand name”

Index contains:
- Name of approved brand (listed alphabetically) - e.g., “Chlor 100 Granular Medicated Premix”
- MIB code and link to CMIB - “CTC”
- Name of medicating ingredient - Chlortetracycline hydrochloride
- Status - Veterinary prescription
# Index of medicating ingredients by brand name

This page is part of the Guidance Document Repository (GDR).


Date Revised October 2018

## Medicating ingredients by brand name

<table>
<thead>
<tr>
<th>Name of approved brand</th>
<th>MIB code</th>
<th>Name of medicating ingredient</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actogain 100</td>
<td>RAC</td>
<td>Ractopamine hydrochloride</td>
<td>Over the counter</td>
</tr>
<tr>
<td><strong>Aureomycin 220 G Granular Medicated</strong></td>
<td><strong>CTC</strong></td>
<td>Chlortetracycline hydrochloride</td>
<td>Veterinary</td>
</tr>
<tr>
<td>Bovatec 20 Lasalocid Sodium Premix</td>
<td>LAS</td>
<td>Lasalocid sodium</td>
<td>Over the counter</td>
</tr>
<tr>
<td>Chlor 50 Medicated Feed Premix</td>
<td>CTC</td>
<td>Chlortetracycline hydrochloride</td>
<td>Veterinary prescription</td>
</tr>
<tr>
<td><strong>Chlor 100 Granular Medicated Premix</strong></td>
<td><strong>CTC</strong></td>
<td>Chlortetracycline hydrochloride</td>
<td>Veterinary prescription</td>
</tr>
</tbody>
</table>
To find CTC using:
Index of medicating ingredients approved by livestock species

Canadian Food Inspection Agency

Index of medicating ingredients approved by livestock species

- Chickens
- Turkeys
- Swine
- Cattle
- Sheep
- Horses
- Fish
- Rabbits

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Search for related documents in the Guidance Document Repository

Date of revision: April 2018
## Index of medicating ingredients approved by livestock species

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Looking for related documents?
Search for related documents in the Guidance Document Repository.

Chickens  
Turkeys  
Swine  

Cattle  
Sheep  
Swine  

Fish  
Rabbits  

### Date of revision: October 2018

#### Medicating Ingredients approved for Cattle

<table>
<thead>
<tr>
<th>Species (class)</th>
<th>Name of medicating ingredient</th>
<th>MIB code</th>
<th>Name of approved brand(s)</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>Decoquinate</td>
<td>DEC</td>
<td>Deccox 6% Premix</td>
<td>Over the counter</td>
</tr>
</tbody>
</table>
| Beef            | Chlortetracycline hydrochloride | CTC      | 1. Aureomycin 220 G Granular Medicated Premix  
2. Chlor 50 Medicated Feed Premix  
3. Chlor 100 Granular Medicated Premix  
4. Deracin 22% Granular Premix | Veterinary prescription |
To find CTC using:
Index of medicating ingredients by name of sponsor/manufacturer

Index contains:
- Name and address of manufacturer or drug proponent/sponsor
  - e.g., “Bio Agri Mix LP”
- Name of approved brand(s) listed under this particular manufacturer
  - e.g., “Chlor 50 Medicated Feed Premix”
- Name of medicating ingredient
  – “Chlortetracycline hydrochloride”
- MIB code and link to the specific MIB
- Drug Identification Number (DIN) of each product (i.e., dilute drug premix)

<table>
<thead>
<tr>
<th>Name of approved brand(s)</th>
<th>Name of medicating ingredient</th>
<th>MIB code</th>
<th>DIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacitracin MD</td>
<td>Bacitracin (as bacitracin methylene disalicylate)</td>
<td>SACH-M</td>
<td>02400317</td>
</tr>
<tr>
<td>Chlor 50 Medicated Feed Premix</td>
<td>Chlortetracycline hydrochloride</td>
<td>CTC</td>
<td>00641824</td>
</tr>
<tr>
<td>Chlor 100 Granular Medicated Premix</td>
<td>Chlortetracycline hydrochloride</td>
<td>CTC</td>
<td>00698210</td>
</tr>
<tr>
<td>Chlor 250 Medicated Premix</td>
<td>Chlortetracycline hydrochloride, Euthymazine and Penicillin</td>
<td>CTP</td>
<td>00641070</td>
</tr>
<tr>
<td>Lincomycin 44 Premix</td>
<td>Lincomycin</td>
<td>UNQ</td>
<td>02085844</td>
</tr>
<tr>
<td>Lincomycin 44 G Premix</td>
<td>Lincomycin</td>
<td>UNQ</td>
<td>02001097</td>
</tr>
<tr>
<td>Lincomycin 10G Premix</td>
<td>Lincomycin</td>
<td>UNQ</td>
<td>02005074</td>
</tr>
<tr>
<td>Lincomycin 110 G Premix</td>
<td>Lincomycin</td>
<td>UNQ</td>
<td>02095882</td>
</tr>
<tr>
<td>Lincomycin Spatimycin 44.4% G Premix</td>
<td>Lincomycin and Spatimycin</td>
<td>UTP</td>
<td>02306038</td>
</tr>
</tbody>
</table>
Chlortetracycline hydrochloride (CTC) – Medicating Ingredient Brochure

This page is part of the Guidance Document Repository (GDR).

Looking for related documents? Search for related documents in the Guidance Document Repository

**Status:** Veterinary prescription required for approved claims

<table>
<thead>
<tr>
<th>Approved livestock species</th>
<th>Approved claim(s) (abbreviated)</th>
<th>Withdrawal time</th>
<th>Name of approved brand(s)</th>
</tr>
</thead>
</table>
| Beef and non-lactating dairy cattle | 1. Aid in the prevention of foot rot | 5 days (meat) | 1. Aureomycin 220 G Granular Medicated Premix  
2. Chlor 50 Medicated Feed Premix  
3. Chlor 100 Granular Medicated Premix  
4. Deracin 22% Granular Premix |
After clicking on the CTC link for “Beef and non-lactating dairy cattle”:

Page contains:

- The approved claim – “As an aid in the prevention of foot rot”
- The level of medicating ingredient in a complete feed – “At a level in the feed such that each animal will receive 0.22 mg of chlortetracycline hydrochloride per kg of body weight per day or 70 mg of chlortetracycline hydrochloride per head per day.”
- Directions for use including prudent use statement (because CTC is a medically important antimicrobial)
- Applicable Cautions and Warnings
- Accepted Compatibilities – In this case there are none
Our scenario: CMIB-compliant medicated feed

- Commercial feed facility will be manufacturing a “Beef Supplement” containing CTC as an aid in the prevention of foot rot.
- The manufactured medicated feed is to be labelled as per the MIB for CTC.
- The medicated ‘Beef Supplement’ is to be mixed on-farm with the remaining feed ingredients at a rate of 25 kg of the medicated supplement per tonne of complete diet including roughage.
- The beef producer provides a daily intake of 6 kg per/head/day of the resulting medicated complete feed containing CTC to his beef cattle, which have an average body weight of 300 kg.
- How many kilograms of CTC product need to be added to the formulation of the medicated beef supplement?
Our scenario: CMIB-compliant medicated feed
Option 1: 70 mg of CTC per head per day

| Dose of CTC (from the MIB): 70 mg/head/day |
| Complete diet daily intake: 6 kg/head/day |
| Inclusion rate of Supplement in complete diet: 0.025 |

(25 kg Supplement/1000 kg of complete diet)

\[
mg \text{ CTC per day in complete diet} = \frac{Dose \text{ per head}}{Intake}
\]

Ex. 70 mg/6 kg = 11.67 mg CTC per kg complete diet

\[
mg \text{ CTC in Supplement} = \frac{Amount \text{ CTC in complete diet}}{Inclusion \text{ rate of Supplement}}
\]

Ex. 11.67 mg/0.025 = 467 mg of CTC per kg of supplement
Our scenario: CMIB-compliant medicated feed
Option 1: 70 mg of CTC per head per day

If we go one step back, how do we determine how much CTC product needs to be added to the medicated supplement that is manufactured by the feed mill?

- The MIB for CTC lists products with 2 different concentrations:
  - Ex. Chlor 50 contains 110 g CTC/kg of premix, whereas Aureomycin 220G has 220 g CTC/kg of premix

- The medicated supplement for beef cattle has a concentration of **467 mg** of chlortetracycline hydrochloride **per kg**

- Then how much of the CTC product needs to be included in the formulation for the medicated beef premix that is manufactured by the feed mill?
Our scenario: CMIB-compliant medicated feed
Option 1: 70 mg of CTC per head per day

\[
\text{kg of CTC product per 1000 kg of Beef Suppl} = \frac{\text{mg of CTC per kg Suppl}}{\text{mg of CTC per kg of DIN Product}} \times 1000 \text{ kg}
\]

To achieve 467 mg of CTC per kg of the Beef Supplement if the concentration of CTC product is 220 g/kg:

\[
\frac{467 \text{ mg CTC per kg supplement}}{220,000 \text{ mg per kg CTC product}} \times 1000 \text{ kg} = 2.12 \text{ kg of CTC product}
\]

To achieve 467 mg of CTC per kg of the Beef Supplement if the concentration of CTC product is 110 g/kg:

\[
\frac{467 \text{ mg of CTC per kg of Beef Supplement}}{110,000 \text{ mg per kg of CTC product}} \times 1000 \text{ kg} = 4.25 \text{ kg of CTC product}
\]
Our scenario: CMIB-compliant medicated feed
Option 2: 0.22 mg CTC per kg BW per day

Average weight of cattle = 300 kg
Dose: 0.22 mg CTC per kg BW
Complete diet **daily intake**: 6 kg/head/day

\[ mg \text{ CTC per head per day} = Dose \text{ in mg/kg} \times BW \text{ in kg} \]
Ex. 0.22 mg/kg BW * 300 kg = 0.66 mg CTC per head per day

\[ mg \text{ CTC per kg of complete diet} = \frac{mg \text{ CTC per head per day}}{\text{complete diet daily intake}} \]
Ex. 66 mg of CTC per head per day ÷ 2 kg of feed per head per day = 33 mg of CTC per kg of complete diet

**So what is the new target concentration of CTC in this medicated supplement?**

- Using the same calculation as before:

\[ mg \text{ CTC in Supplement} = \frac{Amount \text{ CTC in complete diet}}{Inclusion \text{ rate of Supplement}} \]
Ex. 33 mg CTC in complete diet/0.025 = 1320 mg of CTC in the medicated supplement
The Alternative: Off Label Use

• If upon reviewing the MIB for a specific medication and the desired use, level or species is not indicated:
  – The veterinarian may issue an off label prescription (also referred to as Extra Label use)
  – The feed is subject to all the information and labelling requirements specified in Sections 5(g) and 26(7) of the Feeds Regulations
  – The prescription is required to be issued and on hand at the feed mill prior to manufacture of the feed.
Off-label use – a reminder

- When prescribing a medication off label the veterinarian can be considered responsible for any residue violations due to communication of inappropriate withdrawal times.
- Veterinarians are highly recommended to contact CgFARAD for guidance regarding off label withdrawal periods.
When writing a veterinary prescription, **the name** and **inclusion level** of the medicating ingredient must be on the prescription.

On all veterinary prescriptions, the veterinarian **MUST** indicate if brand substitution is allowable or ensure that the particular product that is indicated on the prescription is available at the commercial feed mill where the feed will be manufactured.

Failure to do so may result in prescriptions being returned.
As an example:

<table>
<thead>
<tr>
<th>ANIMALS TO BE TREATED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
</tr>
<tr>
<td>----------</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TREATMENT DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td># Days:</td>
</tr>
<tr>
<td>Feeding Start Date (MM/DD/YYYY):</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MEDICATED FEED INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Feed to be Medicated (Complete/Supplement/Macro):</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name of Feed to be Medicated (if applicable):</th>
<th>Total Quantity of Medicated Feed Product (kg or tonnes):</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Brand Substitution Acceptable?</th>
<th>Yes [ ]</th>
<th>No [ ]</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>DIN product BRAND NAME (Active ingredient, Al;): g of Al/kg of DIN product</th>
<th>g of Al/tonne complete feed</th>
<th>g of DIN product/tonne of complete feed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cautionary note on using the CMIB

• The CMIB is a useful resource for the manufacture and labelling of medicated feed, however it remains your responsibility to be aware of the conditions of use inherent for each medication. For example:

  ➢ If using the CMIB and prescribing multiple medications to be combined into a single feed, be mindful of any conflicting information. In all cases where there are contradictions in the directions, warnings or cautions of the combined medications, the most conservative use and restrictions will apply.
Want to keep up to date on the CMIB?

- You can use the CFIA’s Email Notification Services to get updates emailed directly to you
  - Visit the CFIA’s main web page (www.inspection.gc.ca)
  - Go to very bottom right hand corner of the Agency’s main web page and under the heading “Stay connected”, click on “Email notifications”
  - Under the heading “Sign up for” select “Animal health and feed-related notifications” and enter your information and make your subscription selections
  - A listserv message is sent out to those signed up for the Animal health and feed-related notifications each time the CMIB is updated on the CFIA’s website
    - New additions to the CMIB (DIN products, claims, new medicating ingredients)
    - Removal of DIN products from the CMIB
    - Changes to manufacturers/drug proponents
Do you have Questions about the CMIB?

• Submit your question to:
cfia.afd-daa.acia@canada.ca
WORKING TOGETHER TO PROMOTE THE RESPONSIBLE USE OF ANTIMICROBIALS IN ANIMALS

BACTERIA
Bacteria are everywhere - in the environment, in humans and in animals. Antimicrobial drugs (antibiotics) are used to treat and prevent bacterial infections in humans and animals. Any antimicrobial use can lead to resistance, but the inappropriate use speeds up the development and spread of RESISTANT BACTERIA.

RESISTANT BACTERIA
Resistant bacteria can spread between animals and humans through the food we eat and from human and animal contact. Antimicrobial resistance is a serious public health problem around the world.

WHAT CAN BE DONE?
We all have a role to play to promote the responsible use of antimicrobials, and to prevent human and animal health from the threat of antimicrobial resistance.
Learn more about the action Health Canada is taking to address this problem.

Health Canada
Sané Canada
Canada